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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,525	02/05/2002	Karla Robotti	10011206	2898
22878 7590 03/18/2008 AGILENT TECHNOLOGIES INC. INTELLECTUAL PROPERTY ADMINISTRATION,LEGAL DEPT. MS BLDG. E P.O. BOX 7599 LOVELAND, CO 80537			EXAMINER NGUYEN, QUANG	
			ART UNIT 1633	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

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IPOPS.LEGAL@agilent.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/072,525	<b>Applicant(s)</b> ROBOTTI, KARLA	
	<b>Examiner</b> QUANG NGUYEN, Ph.D.	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 December 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3, 9, 15-21, 24, 26-56, 58 and 59 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 9, 15-21, 24, 26-56 and 58-59 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's amendment filed on 12/07/07 was entered.

Claims 1-3, 9, 15-21, 24, 26-56 and 58-59 are pending in the present application, and they are examined on the merits herein.

### ***Claim Objections***

Claim 43 is still objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This is because in claim 43 which is dependent on claim 1, the sol-gel particle size is from about 1 nm to about 30 nm which is outside the range of 10 um to about 80 um in claim 1.

The examiner notes that claim 43 is still not amended.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 24, 26-27, 33-36, 41-56 and 58-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunn et al. (U.S. Patent 5,200,334; IDS) in view of

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Lochhead et al. (US 6,039,897), Avnir et al. (U.S. Patent 5,300,564; IDS), Avnir et al. (US 6,159,453), and Swedberg et al. (U.S. Patent 6,240,790) for the same reasons already set forth in the Office action mailed on 5/30/07 (pages 4-10). ***The same rejection is restated below. It is further noted that amended claims 45 and 56 are included in the same rejection.***

Dunn et al. teaches a process for the production of a porous, transparent sol-gel glass containing an alcohol sensitive active biological material entrapped therein comprising: (a) forming a single phase sol by mixing a metal alkoxide in a non-alcoholic medium comprising water and an acid catalyst in a container exposed to ultrasonic energy, the mixture having a pH not greater than about 2; (b) removing the ultrasonic energy and raising the pH of the sol to about 5 to 7 by the addition of a buffering agent; (c) adding an alcohol sensitive active biological material to the buffered sol; (d) forming a gel and allowing the gel to age; and (e) allowing at least a portion of the water in the gel to evaporate so that the volume of the product produced in step (d) is decreased and the active biological material is trapped in a monolith of the gel having a reduced volume (see abstract, Fig. 1 and claim 1). Although exemplified method utilizes tetramethylorthosilicate (TMOS), and proteins (e.g., RNase A, proteases, hemoglobin, cytochrome c, metal ion binders, see col. 3, lines 38-59 and Table 1) as active biological materials, however other silicon alkoxides such as tetraethylorthosilicate (TEOS) and other active silicon compounds as well as other metal alkoxides (not limited to aluminium, titanium, zirconium, vanadium, sodium, calcium and boron or combinations thereof can be used (col. 2, line 60 continues to line 10 of col. 3). In an exemplified

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method, the gel is allowed to age at room temperature for 7 to 21 days (col. 5, lines 2-8, 17-19). The porous, transparent sol-gel glass has a median pore radius of about 15 Angstroms (1.5 nm) and a maximum pore radius of about 100 Angstroms or 10 nm (see Fig. 2, claim 22), and in the form of thin films as small as 1000 Angstroms thick or shaped gels having dimensions in its smallest direction of at least 0.5 cm or a monolith (see Summary and col. 2, lines 1-5). Dunn et al. further teaches that **encapsulated or entrapped enzymes are used with increasing frequency as micro-catalysts and analytical devices of very high sensitivity, and that enzymes have been enclosed in membranes systems and used as high-sensitivity monitoring devices. However, such membrane systems are cumbersome and difficult to miniaturize. Therefore, it would be highly advantageous to encapsulate enzymes in a porous, transparent glass structure, such as structures prepared by the sol-gel process. Such an encapsulation would be significantly easier to miniaturize and would be far less cumbersome and far more reliable than membrane encapsulating systems** (col. 1, lines 27-36). Additionally, enzyme encapsulation within a transparent glass structure would allow for the monitoring of many enzymatic reactions by using simple, photometric monitoring systems (col. 1, lines 27-36). Because of the light transmission characteristics of the glasses, UV, IR and visible light optical spectroscopy as well as fluorescence, luminescence, absorption, emission and reflection techniques are all suitable for quantitative and/or qualitative monitoring of chemical changes produced by the sol-gel glasses with entrapped enzymes (col. 4, lines 49-56).

Dunn et al. does not teach explicitly a method of preparing any microanalytical device containing sol-gel particulates comprising an entrapped biological molecule and having a diameter of from about 10 micrometers to about 80 micrometers, or a method of using the same microanalytical device.

However, at the filing date of the present application, Lochhead et al already disclosed a Micro-molding in capillaries (MIMIC) process for **fabricating micronscale structures or devices for use in sensor, waveguide and integrated optics applications using a micro-molding fluid that is a sol that can comprise a variety of biologically active molecules including proteins, enzymes, antibodies, antigens and nucleic acid which bind to, or interact with analytes including other biologically active molecules** (see at least col. 6, lines 9-62). Lochhead et al further taught an exemplified fluid channel that is an element of a micro-fluidic chemical analysis system with appropriate means for fluid sample introduction and a means for detecting indicator response to a particular analyte that may be present in fluid passed through the micro channel (see Fig. 5, and col. 9, lines 37-62). The channel is optically accessible through an optically transparent cover for detection of dye fluorescence (col. 9, lines 37-62). Due to the presence of multiple fluid channels, the micro-fabricated devices of Lochhead et al. are capable of performing high throughput screening of samples. Additionally, the arrangement of multiple independent fluid channels in a microfabricated device can also be considered to be a form of a microarray (see Fig. 1). It is also noted that the term "monolith" means a solid-like body in one piece, and may be from several um in size to greater than tens of mm in size and beyond (page 10,

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lines 27-28). Lochhead et al further teaches that the potential for rapid analysis and portability makes microfabricated devices attractive for applications ranging from remote chemical sensing to medical diagnostics (col. 1, lines 18-22).

Avnir et al. (U.S. Patent 5,300,564) also taught obtaining a chemical interaction between at least one reagent trapped in sol-gel glass by doping it with the reagent, and diffusible solutes or components in an adjacent liquid or gas phase. The reagents, the solutes and the components can be any organic or inorganic compounds or materials of biological origin including enzymes (see abstract). Avnir et al. further taught that the doped sol-gel glass can be in any shape suitable for the test, for example, it can have the shape of rods, discs, cubes, sieves, **powder** or thin films coating conventional glass plates or any other inert solid support (col. 3, lines 20-24). **Avnir et al. also taught that the doped sol gel glasses can be used for all chromatographic purposes including liquid, gas and thin layer chromatography. The extraction or separation is performed by passing the solution through columns made from appropriately doped sol gel material** (col. 3, lines 445-52). **Particularly, Avnir et al. taught that for sol-gel immobilized enzymes, crushed powder sol gel glasses may be used as support for enzymatic column chromatography** (col.5, lines 37-39, and col. 7, lines 55-57).

Avnir et al. (US 6,159,453) also taught that **doped sol-gel particulates or powder in any shape with 0.01-100 microns in diameter** were successfully made for delivering sunscreen molecules (see at least the abstract; col. 2, lines 53-62; col. 4, lines 42-47; col. 6, lines 28-32).

Furthermore, Swedberg et al also taught a high-throughput microanalysis device having a plurality of sample processing compartments for use in analysis of small and/or macromolecular and/or other solutes in the liquid phase (see abstract). The microstructures in the microanalysis device include sample separation means that include electrochromatographic separations performed in columns or microcapillary format (col. 6, line 61 continues to lines 49 of col. 7). Swedberg et al further taught that the microanalysis device is interfaced with any analytical detection means well known in the art, such as UV/Vis, Near IR, fluorescence, refractive index (RI), Raman techniques, as well as Mass spectrometry (MS) and NMR well suited to yielding high quality chemical information for multi-component samples, requiring no a priori knowledge of the constituents (col. 6, lines 3-11).

Accordingly, at the effective filing date of the present application, it would have been obvious for an ordinary skilled artisan in the art to modify the teachings for Dunn et al. by forming a micro-analytical device containing their biological material doped sol-gel particulates or powder having a diameter of about 10 microns to about 80 microns and using such micro-analytical device for use in sensor, waveguide and integrated optics applications and/or analysis of small and/or macromolecular and/or other solutes in the liquid phase in light of the overall teachings of Lochhead et al., Avnir et al. (U.S. Patent 5,300,564), Avnir et al. (US 6,159,453) and Swedberg et al.

An ordinary skilled artisan would have been motivated to carry out the above modification for at least the following reasons: Dunn et al. already taught that encapsulated biological material (e.g., enzymes) prepared by the sol-gel process is

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easier to miniaturize and less cumbersome for use in analytical devices of very high sensitivity; Lochhead et al. already taught the feasibility of fabricating micron-scale devices containing a biological material embedded in a sol-gel at least for sensor, waveguide and integrated optics applications, and microfabriated devices are attractive for applications ranging from remote chemical sensing to medical analysis due to the potential of rapid analysis and portability; Avnir et al already disclosed that doped sol gel glasses for all chromatographic purposes including liquid, gas and thin layer chromatography and doped sol-gel particulates or powder in any shape with 0.01-100 microns in diameter were successfully made and used, and finally Swedberg et al also taught a format of a microdevice containing sample separation means that include electrochromatographic separations performed in columns or microcapillary format that allows high throughput sample processing and analysis of small and/or macromolecular solutes in biological liquids in a truly integrated fashion. In summary, an ordinary skilled artisan would have been motivated to carry out the above modification because the reduction in size of an analytical procedure of technique translates to a reduction in analysis time, costs and paves the way for high-throughput applications.

An ordinary skilled artisan would have a reasonable expectation of success based on the teachings of Dunn et al., Lochhead et al., Avnir et al. (U.S. Patent 5,300,564), Avnir et al. (US 6,159,453) and Swedberg et al., as well a high level of skill of an ordinary skilled artisan in the art.

Accordingly, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

### ***Response to Arguments***

Applicants' arguments with respect to the above rejection in the Amendment filed on 12/07/07 (pages 14-16) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

With respect to the primary reference of Dunn, Applicant argues that the reference reveals a porous sol-gel material and encapsulated enzymes and it has little relating to the instant claims drawn to a method of preparing an analytical device as recited. With respect to the secondary reference of Avnir (5,300,564), Applicant argues that the reference discloses sol-gel glass can be in any shape suitable for test, including a powder, and yet the instant claims feature forming a sol-gel comprising an entrapped biological molecule, crushing the sol-gel to particulate. Applicant further argue that two additional reference are applied to cure deficiencies of Dunn and of Avnir (5,300,564) but without the independent claim 44 as a template, one skilled in the art would not have found it obvious to combine these references, and that a four-way combination of references mandates that impressive hindsight has been applied. Applicant further argues that the Office action has failed to address at least one feature of claim 44, particularly the limitation "forming the sol-gel particulates into a bed within the microanalytical device", and that a review of the Office action does not reveal the alleged disclosure of the bed within a microanalytical device. Similarly, the Office action does not specifically relate the alleged disclosure within the applied art of the features of independent claim 58 having features similar to those of claim 44. Accordingly,

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independent claims 44, 58 and dependent claims thereof are patentable over the prior art.

Firstly, it should be noted that the above rejection is based on the totality of the teachings of Dunn, Lochhead, Avnir (5,300,564), Avnir (6,159,453) and Swedberg; and not on selected teachings of Dunn and Avnir (5,300,564) in isolation. It is also apparent that Applicant did not any teachings of Lochhead into consideration.

Secondly, in response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). Furthermore, it should be noted that the number of references used in the above rejection is dictated by the number of limitations recited in the instant claims.

Thirdly, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In the above rejection, Dunn taught clearly that it would be highly advantageous to encapsulate enzymes in a porous, transparent glass structure, such as structures

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prepared by the sol-gel process; and that such encapsulation would be significantly easier to miniaturize, far less cumbersome and far more reliable to be used in analytical devices of very high sensitivity. At the filing date of the present application, Lochhead already taught fabricating micronscale structures and devices for use in sensor, waveguide and integrated optics applications using a micro-molding fluid that is a sol comprising a variety of biological active molecules including proteins, enzymes, antibodies, antigens, nucleic acids to bind to or interact with analytes. Moreover, Avnir (5,300,564) also taught the use of doped sol-gel glass (including sol-gel immobilized enzymes) in various shape such as rods, discs, cubes, sieves, powder, thin coating films for all chromatographic purposes including liquid, gas, thin layer chromatography, particularly as support for enzymatic column chromatography. It should be noted that a powder contains particles or particulates. Alternatively, rods, discs, cubes, sieves can also be considered to fall within the breadth of the term "particulates". Avnir (6,159,453) already taught that **doped sol-gel particulates or powder in any shape with 0.01-100 microns in diameter were successfully made for delivering sunscreen molecules.** Finally, Swedberg taught a high-throughput microanalytical device for use in analysis of small and/or macromolecular and/or other solutes in the liquid phase, that includes chromatographic separations performed in columns or microcapillary format in a truly integrated fashion. Accordingly, it would have been obvious for an ordinary skilled artisan to modify the teachings for Dunn et al. by forming a micro-analytical device containing biological material doped sol-gel particulates or powder having a diameter of about 10 microns to about 80 microns and using such micro-analytical

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device for use in sensor, waveguide and integrated optics applications and/or analysis of small and/or macromolecular and/or other solutes in the liquid phase in light of the overall teachings of Lochhead et al., Avnir et al. (U.S. Patent 5,300,564), Avnir et al. (US 6,159,453) and Swedberg et al. for the motivations set forth in the above rejection, namely due to the potential for rapid analysis (high throughput analysis), portability as well as a truly integrated fashion offered by a microanalytical or micronscale structures or devices.

Fourthly, with respect to the limitation "forming the sol-gel particulates into a bed within the microanalytical device", by forming a micro-analytical device containing biological material doped sol-gel particulates or powder having a diameter of about 10 microns to about 80 microns as support for column chromatography (columns or microcapillaries) would meet such limitation.

Accordingly, claims 1-3, 24, 26-27, 33-36, 41-56 and 58-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunn et al. in view of Lochhead et al., Avnir et al. (U.S. Patent 5,300,564; IDS), Avnir et al. (US 6,159,453), and Swedberg et al. for the reasons set forth above.

Amended claims 1, 9, 15-21, 28-32, 37-40 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunn et al. (U.S. Patent 5,200,334; IDS) in view of Lochhead et al. (US 6,039,897), Avnir et al. (U.S. Patent 5,300,564; IDS), Avnir et al. (US 6,159,453), and Swedberg et al. (U.S. Patent 6,240,790) as applied to claims 1-3, 24, 26-27, 33-36, 41-56 and 58-59 above, and further in view of Liu et al (US

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6,303,290; IDS) and Reetz et al. (Biotechnology and Bioengineering, Vol. 9:527-534, 1996) for the same reasons already set forth in the Office action mailed on 5/30/07 (pages 10-12). ***The same rejection is restated below.***

The teachings of Dunn et al., Lochhead et al., Avnir et al (US 5,300,564), Avnir et al (US 6,159,453) and Swedberg et al have been discussed above. However, none of the references teaches specifically the making of a porous, inorganic matrix containing a biological material encapsulated therein comprised of colloidal silica sol and dissolved sodium silicate or a tetralkyl orthosilicate and a substituted silane as recited.

However, at the effective filing date of the present application, Liu et al already taught an alcohol-free method of making a porous, inorganic matrix containing a biological material (e.g., RNA, DNA, active proteins, active fragments of DNA, RNA, proteins, enzymes such as RNase, DNase, nuclease, kinase, transferase, trypsin, chymotrypsin, cytochrome c (MW of 12,327) encapsulated therein comprised of colloidal silica sol and dissolved sodium silicate suitable for quantitative or qualitative detection of a test substance that reacts with or whose reaction is catalyzed by an active biological material (col. 3, lines 47-67; col. 4, lines 1-28; col. 4, line 62 continues to line 17 of col. 5). Liu et al further taught that unlike the conventional silica-based, metal alkoxide methods, the types of biopolymers that can be incorporated in the porous, inorganic matrix composites are essentially unlimited due to the completely elimination of alcohol in the process of making (col. 3, lines 34-45).

Additionally, Reetz et al. also taught that lipase activity for lipases entrapped in sol-gels prepared from a mixture of tetramethoxysilane (TMOS) and

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alkyltrimethoxysilanes  $\text{Rsi}(\text{OCH}_3)_3$  **was dramatically enhanced** with increasing amount and alkyl chain length of the hydrophobic silanes, including the alkyl group  $\text{C}_{18}$  (page 529, right-handed column, first complete paragraph and Figure 1).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to further modify the method taught by Dunn et al., Lochhead et al., Avnir et al (US 5,300,564), Avnir et al (US 6,159,453) and Swedberg et al by using a sodium silicate or a substituted silane in the process of immobilizing an enzyme, particularly a lipase, or other biological material in a sol-gel containing colloidal silica sol, in light of the above teachings of Liu et al., and Reetz et al.

An ordinary skilled artisan would have been motivated to carry out the above modifications because of the advantages offered by a porous, inorganic matrix composites comprised of colloidal silica sol and dissolved sodium silicate taught by Liu et al., namely essentially unlimited types of biopolymers can be incorporated and that the denaturation of many biopolymers can be avoided due to the completely elimination of alcohol in the process of making. Additionally, Reetz et al. taught that increasing amount and alkyl chain length of the hydrophobic silanes, including the alkyl group  $\text{C}_{18}$  enhance the activity and/or stability at least for lipase-doped sol-gel.

An ordinary skilled artisan would have a reasonable expectation of success based on the teachings of Dunn et al., Lochhead et al., Avnir et al (US 5,300,564), Avnir et al (US 6,159,453), Swedberg et al, Liu et al., and Reetz et al., as well a high level of skill of an ordinary skilled artisan in the art.

Accordingly, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

### ***Response to Arguments***

Applicant's arguments with respect to the above rejection in the Amendment filed on 12/07/07 (page 16) have been fully considered but they are respectfully not found persuasive.

Applicant argues basically that the instant claims are patentable over the same cited references for the reasons set forth in the rejection of claims 1-3, 24, 26-27, 33-36, 41-56 and 58-59 above.

Please refer to the Examiner's responses to Applicant's same arguments in the rejection of claims 1-3, 24, 26-27, 33-36, 41-56 and 58-59 above.

### ***Conclusions***

***No claim is allowed.***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Voitach, Ph.D., may be reached at (571) 272-0739.

**To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.**

**Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.**

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN, Ph.D./  
Primary Examiner, Art Unit 1633